NERL Research Abstract

EPA's National Exposure Research Laboratory
GPRA Goal 2 - Clean and Safe Water

Significant Research Findings

Method for Identifying Arsenic Species in Urine for Use in Exposure and Epidemiology Studies

Purpose

Humans are exposed to arsenic primarily through drinking water and dietary ingestion. The most commonly found arsenic species are in six different chemical forms: arseno-betaine (AsB), arseno-choline (AsC), dimethyl arsenic acid (DMA), monomethyl arsonic acid (MMA), arsenite (As(III)), and arsenate (As(V)). The toxicity of exposure is strongly dependent on dose and chemical form (As(III) versus AsB) of the arsenic ingested. However, the application of traditional analytical methods for the quantification of arsenic results in a total arsenic concentration. Because this methodology does not differentiate between more toxic forms of arsenic (e.g., inorganic arsenic) and less toxic forms of arsenic (e.g., AsB or AsC), a total arsenic concentration will cause an overestimation of the risk from exposure sources containing only less toxic forms.

Once ingested by humans, arsenic is predominately excreted in urine. The ability to separate arsenic into its chemical forms from a urinary sample would provide valuable information regarding the dose and the source of the arsenic exposure. Because of the lack of methodology to measure the various forms of arsenic, arsenic speciation was identified in the Office of Research and Development's Arsenic Research Plan as a high priority. Thus, research was conducted to develop an analytical approach capable of providing chemical form-specific information in a urinary sample that could then be utilized in future epidemiology studies to assess an individual's exposure to arsenic. Specifically, this analytical methodology provides epidemiologists and risk assessors with improved capabilities for measuring and associating arsenic exposures with observed adverse health effects. The goal of this research was to develop a methodology that provides excellent sensitivity and selectivity, good matrix (urinary sample) tolerance, and chromatographic resolution in combination with reasonable analysis time.

Research Approach

Ion chromatography (IC) coupled with Inductively Coupled Plasma Mass Spectrometry (ICP-MS) detection is one of the premier analytical techniques in arsenic speciation because it combines both the separation strength of IC and

the parts-per-trillion detection capability of ICP-MS. The two sample introduction approaches investigated were direct nebulization and hydride generation. Direct nebulization offers experimental simplicity by allowing a direct coupling of the IC to the ICP-MS, but requires chromatography to separate the arsenic species found in the urine sample from the chloride ion also found in urine. However, if hydride generation is used as the sample introduction approach, the chromatographic separation of the chloride ion from the arsenicals is not required. Hydride generation, in effect, eliminates the chloride ion as a source of interference, and, in doing so, eliminates a source of false positives via increased detector selectivity. This added selectivity is achieved at the expense of added instrumental complexity.

Major Findings and Significance	The publications listed in this abstract outline an analytical approach for speciating arsenic in urine. The major developments from this research are listed below. (1) The development of a membrane hydride generation ICP-MS system that can provide arsenic speciation data in a urine matrix at the low parts-per-trillion concentration range. This inherent sensitivity allows the complex matrix associated with urine to be diluted, and thus alleviates the chromatographic problems associated with the high salt concentrations typical of urine samples. (2) The development of a complementary direct nebulization procedure provides an experimentally simpler approach that could be used by routine testing or non-research oriented laboratories. (3) The development of a photo-oxidation hydride system that provides the means to detect all arsenicals in the urine sample, including exposure source information that may indicate individual dietary patterns (e.g., high AsB and AsC indicates high seafood ingestion). If the photo-oxidation step is omitted (turning the UV lamp off), then only the more toxic arsenicals are detected, thereby providing an analysis that more directly reflects the potential for risk.
Publications	Wei, X.-Y., Brockhoff-Schwegel, C.A., Creed, J.T. Application of sample pre-oxidation of arsenite in human urine prior to speciation via on-line photo-oxidation with membrane hydride generation and ICP-MS detection. *Analyst* 125: 1215-1220, 2000. Wei, X.-Y., Brockhoff-Schwegel, C.A., Creed, J.T. A comparison of urinary arsenic speciation via direct nebulization and on-line photo-oxidation hydride generation with IC separation and ICP-MS detection. *Journal of Analytical Atomic Spectrometry*. Submitted.
Future Research	Recent literature reports indicate that the ingestion of arsenosugars (predominately associated with seafood ingestion) can produce metabolites of the arsenosugars. To date, these metabolites have not been structurally identified, and their potential toxicity is not known. The identification and elution characteristics of these metabolites in urine, including MMA(III) and

DMA(III), is an area needing additional research.

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